NMCP COVID-19 Literature Report #30: Friday, 17 July 2020

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Purpose: These reports are curated collections of current research, evidence reviews, and news regarding the COVID-19 pandemic; they are biweekly, planned for Tuesdays and Fridays. Please feel free to reach out with questions and suggestions for future topics.

All reports are available online at https://nmcp.libguides.com/covidreport. Access is private; you will need to use the direct link or bookmark the URL, along with the case-sensitive password "NMCPfinest".

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, things are changing rapidly, with new research and potentially conflicting literature published daily.

Statistics

Global

13,841,890 confirmed cases and 590,845 deaths in 188 countries/regions

United States*

top 5 states by cases (Virginia is ranked 15th)

	TOTAL US	NY	CA	FL	TX	NJ
Confirmed Cases	3,578,593	404,775	364,835	315,775	305,854	176,501
Tested	43,351,945	4,921,210	5,915,508	2,815,618	2,699,855	1,759,904
Recovered	NA	71,867	NA	NA	155,937	31,400
Deaths	138,384	32,446	7,490	4,677	3,657	15,665

^{*}see census.gov for current US Population data; NA: not all data available

JHU CSSE as of 1100 EDT 17 July 2020

Virginia	Total	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	75,433	1,560	625	984	2,020	872	676	2,396
Hospitalized	7,087	163	42	52	137	96	70	142
Deaths	2,013	24	4	10	19	20	44	34

VA DOH as of 1100 EDT 17 July 2020

Summaries from Other Sources

<u>CEBM</u>: SARS-CoV-2 and the Role of Orofecal Transmission: Evidence Brief (16 July, published online 17 July 2020)

"Various observational and mechanistic evidence presented throughout this evidence brief, support the hypothesis that SARS-CoV-2 can infect and be shed from the human gastrointestinal tract....

A review of 29 relevant studies (23 published and 6 preprints) reported that approximately 12% of patients with SARS-CoV-2 infection reported gastrointestinal symptoms, including diarrhoea, nausea, and vomiting. Eight included studies reported the detection of viral RNA of SARS-CoV-2 in stool and the pooled analysis reported that RNA shedding in stool was detected in up to 41% of COVID-19 patients."

Selected Primary Literature

Recently published in peer-reviewed journals

MMWR: Symptom Profiles of a Convenience Sample of Patients with COVID-19 — United States, January—April 2020 (17 July 2020)

"Information about COVID-19 symptoms, especially among nonhospitalized U.S. patients, is limited and not well characterized across the spectrum of illness severity.

Fever, cough, or shortness of breath were commonly reported among a convenience sample of U.S. COVID-19 patients with symptom onset during January—April and a range of illness severity; gastrointestinal symptoms and other symptoms, such as chills, myalgia, headache, and fatigue, also were commonly reported.

U.S. COVID-19 patients report a wide range of symptoms across a spectrum of illness severity; these findings can inform clinical case definitions or testing guidance to aid prompt recognition to slow the spread of COVID-19."

MMWR: Detection and Genetic Characterization of Community-Based SARS-CoV-2 Infections — New York City, March 2020 (17 July 2020)

"To limit SARS-CoV-2 introduction, the United States restricted travel from China on February 2 and from Europe on March 13, 2020. By March 15, community transmission was widespread in New York City (NYC).

The NYC Department of Health and Mental Hygiene conducted sentinel surveillance of influenza-like symptoms (ILS) and genetic sequencing to characterize community transmission and determine the geographic origin of SARS-CoV-2 infections. Among 544 specimens tested from persons with ILS and negative influenza test results, 36 (6.6%) were

positive. Genetically sequenced positive specimens most closely resembled sequences circulating in Europe.

Partnering with health care facilities and establishing systems for sentinel surveillance with capacity for genetic sequencing before an outbreak can inform timely public health response strategies."

MMWR: Factors Associated with Cloth Face Covering Use Among Adults During the COVID-19 Pandemic — United States, April and May 2020 (17 July 2020; early release 14 July 2020)

"On April 3, 2020, the White House Coronavirus Task Force and CDC recommended that persons wear a cloth face covering in public to slow the spread of COVID-19.

After the initial recommendation was released, high rates of cloth face covering use were reported in the United States. An increase in the rate of cloth face covering use was observed from April to May and was sustained, particularly among non-Hispanic blacks and other races, Hispanics, persons aged ≤39 years, and persons living in the Northeast.

Public health messages should target audiences not wearing cloth face coverings and reinforce positive attitudes, perceived norms, personal agency, and physical and health benefits of obtaining and wearing cloth face coverings consistently and correctly."

<u>Lancet</u>: Histopathology and ultrastructural findings of fatal COVID-19 infections in Washington State: a case series (16 July 2020)

"This study provides crucial information related to the natural history of fatal COVID-19 from early in the US outbreak. Our analysis used multiple methods, including clinical chart review, histopathological evaluation, electron microscopy, immunohistochemistry, and quantitative RT-qPCR to examine all major organ systems. To our knowledge, no previous studies have used all these techniques simultaneously. Our results support previous studies, which suggested that diffuse alveolar damage is the major source of pulmonary injury in COVID-19; however, we found no evidence of widespread microvascular injury. Additional investigations raised the possibility of extrapulmonary involvement in renal, intestinal, cardiac, and lymphoid tissues.

In addition to the results of previous studies, our findings provide a histological explanation for physiological derangements observed by clinicians in patients who died with COVID-19. Further investigation is required to characterise the extent of extrapulmonary injury caused by severe acute respiratory syndrome coronavirus 2 infection."

<u>Lancet Psychiatry</u>: How mental health care should change as a consequence of the COVID-19 pandemic (16 July 2020)

"The unpredictability and uncertainty of the COVID-19 pandemic; the associated lockdowns, physical distancing, and other containment strategies; and the resulting economic breakdown could increase the risk of mental health problems and exacerbate health

inequalities. Preliminary findings suggest adverse mental health effects in previously healthy people and especially in people with pre-existing mental health disorders. Despite the heterogeneity of worldwide health systems, efforts have been made to adapt the delivery of mental health care to the demands of COVID-19. Mental health concerns have been addressed via the public mental health response and by adapting mental health services, mostly focusing on infection control, modifying access to diagnosis and treatment, ensuring continuity of care for mental health service users, and paying attention to new cases of mental ill health and populations at high risk of mental health problems. Sustainable adaptations of delivery systems for mental health care should be developed by experts, clinicians, and service users, and should be specifically designed to mitigate disparities in health-care provision. Thorough and continuous assessment of health and service-use outcomes in mental health clinical practice will be crucial for defining which practices should be further developed and which discontinued. For this Position Paper, an international group of clinicians, mental health experts, and users of mental health services has come together to reflect on the challenges for mental health that COVID-19 poses. The interconnectedness of the world made society vulnerable to this infection, but it also provides the infrastructure to address previous system failings by disseminating good practices that can result in sustained, efficient, and equitable delivery of mental health-care delivery. Thus, the COVID-19 pandemic could be an opportunity to improve mental health services."

Nature: Reconstruction of the full transmission dynamics of COVID-19 in Wuhan (16 July 2020)

"As countries in the world review interventions for containing the COVID-19 pandemic, important lessons can be drawn by studying the full transmission dynamics of SARS-CoV-2 in Wuhan, China, where vigorous non-pharmaceutical interventions have suppressed the local COVID-19 outbreak. Here, we use a modelling approach to reconstruct the full-spectrum dynamics of COVID-19 between January 1, 2020 and March 8, 2020 across five periods marked by events and interventions based on 32,583 laboratory-confirmed cases. Accounting for presymptomatic infectiousness, time-varying ascertainment rates, transmission rates and population movements, we identify two key features of the outbreak: high covertness and high transmissibility. We estimate 87% (lower bound 53%) of the infections before March 8 were unascertained, potentially including asymptomatic and mild-symptomatic cases; and a basic reproduction number R0 of 3.54 (95% credible interval [CrI]: 3.40-3.67) in the early outbreak, much higher than for SARS and MERS. We observe that multi-pronged interventions had considerable positive effects on controlling the outbreak, decreasing the reproduction number to 0.28 (0.23-0.33) and by projection reducing the total infections in Wuhan by 96.0% as of March 8. We furthermore explore the probability of resurgence following lifting of all interventions after 14 days of no ascertained infections, estimating it at 0.32 and 0.06 based on models with 87% and 53% unascertained infections, respectively, highlighting the risk posed by unascertained cases in changing

intervention strategies. These results provide important implications for continuing surveillance and interventions to eventually contain COVID-19 outbreaks."

<u>Disaster Med Public Health Prep:</u> Clinical features of fatalities in patients with COVID-19 (15 July 2020)

"The novel coronavirus (COVID-19) pandemic has spread over 213 countries and territories. We sought to describe the clinical features of fatalities in patients with severe COVID-19 in an internet-based retrospective cohort study through retrieving the clinical information of 100 COVID-19 deaths from non-duplicating incidental reports in Chinese provincial and other governmental websites between January 23 and March 10, 2020. About 6 of 10 COVID-19 deaths were males (64.0%). The average age was 70.7±13.5 years, and 84% of patients were elderly (over age 60 y). The mean duration from admission to diagnosis was 2.2±3.8 days (median: 1). The mean duration from diagnosis to death was 9.9±7.0 days (median: 9). About 3 of 4 cases (76.0%) were complicated by 1 or more chronic diseases, including hypertension (41.0%), diabetes (29.0%) and coronary heart disease (27.0%), respiratory disorders (23.0%) and cerebrovascular disease (12.0%). Fever (46.0%), cough (33.0%), shortness of breath (9.0%) were the most common first symptoms. Multiple organ failure (67.9%), circulatory failure (20.2%) and respiratory failure (11.9%) are the top three direct causes of death. COVID-19 deaths are mainly elderly and patients with chronic diseases especially cardiovascular disorders and diabetes. Multiple organ failure is the most common direct cause of death."

<u>JAMA Intern Med</u>: Factors Associated With Death in Critically III Patients With Coronavirus Disease 2019 in the US (15 July 2020)

"Question: What are the characteristics, outcomes, and factors associated with death among critically ill patients with coronavirus disease 2019 (COVID-19) in the US?

Findings: In a cohort of 2215 adults with COVID-19 who were admitted to intensive care units at 65 sites, 784 (35.4%) died within 28 days, with wide variation among hospitals. Factors associated with death included older age, male sex, obesity, coronary artery disease, cancer, acute organ dysfunction, and admission to a hospital with fewer intensive care unit beds.

Meaning: This study identified demographic, clinical, and hospital-level factors associated with death in critically ill patients with COVID-19 that may be used to facilitate the identification of medications and supportive therapies that can improve outcomes."

JAMA Dermatol: Enanthem in Patients With COVID-19 and Skin Rash (15 July 2020)

Researchers in Spain found 6 of 21 patients with COVID-19 and an exterior skin rash also had oral involvement, which seemed to appear about 2 weeks after symptom onset.

<u>Nature</u>: SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls (15 July 2020)

"Memory T cells induced by previous pathogens can shape the susceptibility to, and clinical severity of, subsequent infections. Little is known about the presence of pre-existing memory T cells in humans with the potential to recognize SARS-CoV-2. Here, we first studied T cell responses to structural (nucleocapsid protein, NP) and non-structural (NSP-7 and NSP13 of ORF1) regions of SARS-CoV-2 in COVID-19 convalescents (n=36). In all of them we demonstrated the presence of CD4 and CD8 T cells recognizing multiple regions of the NP protein. We then showed that SARS-recovered patients (n=23) still possess long-lasting memory T cells reactive to SARS-NP 17 years after the 2003 outbreak, which displayed robust cross-reactivity to SARS-CoV-2 NP. Surprisingly, we also frequently detected SARS-CoV-2 specific T cells in individuals with no history of SARS, COVID-19 or contact with SARS/COVID-19 patients (n=37). SARS-CoV-2 T cells in uninfected donors exhibited a different pattern of immunodominance, frequently targeting the ORF-1-coded proteins NSP7 and 13 as well as the NP structural protein. Epitope characterization of NSP7-specific T cells showed recognition of protein fragments with low homology to "common cold" human coronaviruses but conserved amongst animal betacoranaviruses. Thus, infection with betacoronaviruses induces multispecific and long-lasting T cell immunity to the structural protein NP. Understanding how pre-existing NP- and ORF-1-specific T cells present in the general population impact susceptibility and pathogenesis of SARS-CoV-2 infection is of paramount importance for the management of the current COVID-19 pandemic."

<u>JAMA</u>: Association Between Universal Masking in a Health Care System and SARS-CoV-2 Positivity Among Health Care Workers (14 July 2020)

"Mass General Brigham (MGB) is the largest health care system in Massachusetts, with 12 hospitals and more than 75,000 employees. In March 2020, MGB implemented a multipronged infection reduction strategy involving systematic testing of symptomatic HCWs [healthcare workers] and universal masking of all HCWs and patients with surgical masks. This study assessed the association of hospital masking policies with the SARS-CoV-2 infection rate among HCWs....

Of 9850 tested HCWs, 1271 (12.9%) had positive results for SARS-CoV-2 (median age, 39 years; 73% female; 7.4% physicians or trainees, 26.5% nurses or physician assistants, 17.8% technologists or nursing support, and 48.3% other)....

Universal masking at MGB was associated with a significantly lower rate of SARS-CoV-2 positivity among HCWs. This association may be related to a decrease in transmission between patients and HCWs and among HCWs."

NEJM: An mRNA Vaccine against SARS-CoV-2 — Preliminary Report (14 July 2020)

"We conducted a phase 1, dose-escalation, open-label trial including 45 healthy adults, 18 to 55 years of age, who received two vaccinations, 28 days apart, with mRNA-1273 in a dose of 25 μ g, 100 μ g, or 250 μ g. There were 15 participants in each dose group.

After the first vaccination, antibody responses were higher with higher dose (day 29 enzyme-linked immunosorbent assay anti–S-2P antibody geometric mean titer [GMT], 40,227 in the 25- μ g group, 109,209 in the 100- μ g group, and 213,526 in the 250- μ g group). After the second vaccination, the titers increased (day 57 GMT, 299,751, 782,719, and 1,192,154, respectively). After the second vaccination, serum-neutralizing activity was detected by two methods in all participants evaluated, with values generally similar to those in the upper half of the distribution of a panel of control convalescent serum specimens. Solicited adverse events that occurred in more than half the participants included fatigue, chills, headache, myalgia, and pain at the injection site. Systemic adverse events were more common after the second vaccination, particularly with the highest dose, and three participants (21%) in the 250- μ g dose group reported one or more severe adverse events.

The mRNA-1273 vaccine induced anti–SARS-CoV-2 immune responses in all participants, and no trial-limiting safety concerns were identified. These findings support further development of this vaccine."

<u>JAMA Netw Open</u>: Characteristics of the Multiplicity of Randomized Clinical Trials for Coronavirus Disease 2019 Launched During the Pandemic (13 July 2020)

"We performed a data query of the ClinicalTrials.gov registry for interventional trials in any clinical phase regarding COVID-19 on June 8, 2020....

We found a high rate of trial multiplicity, particularly with chloroquines, which are being tested in 143 studies. Although these overlapping trials may afford opportunities for replication and validation, the high degree of multiplicity also enhances the likelihood of finding a positive result through chance alone, potentially resulting in widespread use of an ineffective and possibly hazardous intervention.

The fragmentation of efforts could also lead to unnecessary competition for participants, which potentially compromises trial accrual and statistical power for all trials."

<u>Science</u>: Impaired type I interferon activity and inflammatory responses in severe COVID-19 patients (13 July 2020)

"Coronavirus disease 2019 (COVID-19) is characterized by distinct patterns of disease progression suggesting diverse host immune responses. We performed an integrated immune analysis on a cohort of 50 COVID-19 patients with various disease severity. A unique phenotype was observed in severe and critical patients, consisting of a highly impaired interferon (IFN) type I response (characterized by no IFN- β and low IFN- α

production and activity), associated with a persistent blood viral load and an exacerbated inflammatory response. Inflammation was partially driven by the transcriptional factor NF- κB and characterized by increased tumor necrosis factor (TNF)- α and interleukin (IL)-6 production and signaling. These data suggest that type-I IFN deficiency in the blood could be a hallmark of severe COVID-19 and provide a rationale for combined therapeutic approaches."

Preprints—not yet peer-reviewed papers

<u>arXiv</u>, <u>bioRxiv</u>, and <u>medRxiv</u> are preprint servers: "[T]hese are preliminary reports that have not been peer-reviewed. They should not be relied on to guide clinical practice or health-related behavior and should not be reported in news media as established information."

<u>medRxiv</u>: SARS-CoV-2 infection induces robust, neutralizing antibody responses that are stable for at least three months (posted 17 July 2020)

"SARS-CoV-2 has caused a global pandemic with millions infected and numerous fatalities. Questions regarding the robustness, functionality and longevity of the antibody response to the virus remain unanswered. Here we report that the vast majority of infected individuals with mild-to-moderate COVID-19 experience robust IgG antibody responses against the viral spike protein, based on a dataset of 19,860 individuals screened at Mount Sinai Health System in New York City. We also show that titers are stable for at least a period approximating three months, and that anti-spike binding titers significantly correlate with neutralization of authentic SARS-CoV-2. Our data suggests that more than 90% of seroconverters make detectible neutralizing antibody responses and that these titers are stable for at least the near-term future."

News in Brief

"There was a time in the United States when 40,000 coronavirus cases in a day seemed like an alarming milestone. That was less than three weeks ago. Now, the number of new infections reported each day is reaching dizzying new heights. On Thursday [16 July 2020], the daily U.S. caseload topped 70,000 for the first time, according to data tracked by The Washington Post." (WaPo)

Big Changes to Reporting COVID Data

As of Wednesday, 15 July, a new directive from the current administration requires hospitals to bypass the CDC and report all COVID-19 patient information to a central database in Washington, DC (NYT).

The data, which go to HHS, will no longer be publically available; information on hospital capacity, inpatient bed and ICU bed occupancy have been removed from the CDC website (Beckers).

Some warn that this change and reporting will increase burden on facilities already strained by the pandemic (WaPo).

This change in reporting has caused problems and significant challenges at tracking cases and monitoring hospital utilization for many -- for example, Idaho can no longer update their dashboard because it was based on data from the CDC (<u>Statesman</u>).

"How HHS's new hospital data reporting system will actually affect the US COVID-19 response" (STAT).

Reopening Issues

Starting on Monday, 20 July, Walmart nationwide will require shoppers to wear a mask (<u>USA Today</u>). Target and CVS will also require masks (<u>NPR</u>).

The governor of Georgia has signed an execute order that local governments cannot mandate or enforce the wearing of masks; instead, residents and visitors are "strongly encouraged to wear face coverings as practicable" when in public except when eating, drinking or exercising outdoors (Hill).

A report from the National Academies states that schools should prioritize reopening in the fall, especially for grades K-5, and provide significant resources such as masks, cleaning supplies, upgrades ,and other resources to districts and schools (NAP).

Projections and Research

A newly revised University of Washington model projects 224,000 deaths from COVID-19 in the US by November (Reuters).

"Many studies needed to quell this and future pandemics are not being done, and the chance is ebbing away" (Nature).

Testing, Treatments, and Vaccines

According to a new report and action plan from the Rockefeller Foundation, \$75 billion is needed to fix the flawed diagnostic testing and tracing system in the US (RF).

Rwanda is offering free testing and robot caregivers, a program seen as a COVID-19 success story (NPR).

A 2013 study that suggested a beneficial effect of low-dose radiation to treat pneumonia is gaining new life with COVID-19 (STAT; see YJBM for full text of 2013 article).

Russian hackers are trying to steal vaccine and research data from academic and pharmaceutical institutions, according to cybersecurity report from the UK, US, and Canada (Reuters).

Some experts say a coronavirus vaccine administered nasally may be more effective and protective, but it won't be ready quickly (NYT).

Long read: "Covid Vaccine Front-Runner Is Months Ahead of Her Competition" (Bloomberg).

Mis/Disinformation

A man in California is charged with mail fraud and false marketing after claiming the herbal mixture called 'Emergency D-Virus Plan of Care' was FDA approved to treat COVID-19 (DOJ).

An Australian clothing company Lorna Jane has been fined ~\$28,000 USD for marketing 'anti-virus activewear' (Aus TGA).

Other Things to Worry About

WHO officials have confirmed 4 more Ebola cases in the Democratic Republic of the Congo (DRC) Equateur province, bringing the number of cases to 56 and passing the total of the 2018 outbreak in the same area (WHO).

It's hurricane season, and the CDC has a site about how to prepare for natural disasters and severe weather during the pandemic (CDC).

Blast from the Past

A 20-photo collection highlights the influenza masks of 1918, with some Navy history: #14 shows corpsmen at the US Navy hospital in Mare Island, CA; and #17 shows the influenza ward at Walter Reed hospital (Atlantic).

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Statistics

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